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UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
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OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

M.C. Meinert, Esq.
Genetics Institute, Inc.
Legal Affairs
87 CambridgePark Drive
Cambridge, MA 02140

In Re: Patent Term Extension
Application for
U.S. Patent No. 5,171,569
Filed: March 6, 1997

NOTICE OF INFORMALITIES

The above-identified application for patent term extension is considered informal because the application does not provide an adequate explanation of the manner in which each applicable patent claim reads on the approved product or a method of using or making the approved product in compliance with 37 CFR 1.740(a)(9).

37 CFR 1.740(a)(9) requires:

> A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which each applicable patent claim reads on the approved product or a method of using or manufacturing the approved product. (Emphasis added.)

On page 3 of the application for patent term extension, applicant states:

> As required by 37 CFR §1.740(a), the Applicant states that U.S. Patent No. 5,171,569 claims factor IX, a major component of the product (claims 1 and 2) and a method of using (claims 3 and 4).
>
> The licensee, Genetics Institute, Inc., cultures, in its licensed manufacturing facility, Chinese Hamster Ovary cells (CHO cells) that have been transformed with DNA encoding factor IX and recovers from the culture Factor IX protein having procoagulant activity. The protein is purified, concentrated, and formulated by the licensee, Genetics Institute, Inc. to produce the product "rFIX."

Claim 1 of the patent states:

> A plasma-free preparation ... comprising as active ingredient biologically active recombinant DNA-derived factor IX protein derived from a single human individual and which ... normal human plasma.

It is unclear from the application whether rFIX is made from factor IX protein derived from a single human individual and whether the factor IX protein of the approved product meets the conditions of the claim, particularly conditions (1) - (3) that are set forth in the claim. How the

claims read on the approved product must be demonstrated. Normally CHO cells are grown in a bovine serum and such serum would contain plasma. The application states that the protein is purified, but does not address whether the resulting product is plasma free as required by the claim. Is the approved product plasma free? Applicant appears to state that the factor IX protein used to make the approved product is made from CHO cells. Has the CHO cell line been transfected with a single human's DNA?

A demonstration of the manner in which each patent claim reads on the approved product or a method of using of manufacturing the approved product in compliance with 37 CFR 1.740(a)(9) is required.

Clarification is requested of the particular statute(s) under which regulatory review occurred. While applicant states that regulatory review occurred under sections 201 *et seq.* of the Public Health Service Act, it would appear that regulatory review occurred under section 351 of the Public Health Service Act and section 505 of the Federal Food Drug and Cosmetic Act. Note 35 U.S.C. § 156(g)(1)(B).

Applicant has **ONE MONTH** from the date of this letter in order to file the required demonstration. Extensions of time under 37 CFR 1.136 are available. Failure to respond will result in the application for patent term extension being processed as an informal application. Alternatively, applicant may have the holding of informality reviewed as set forth in 37 CFR 1.740(c).

Correspondence with respect to this matter should be addressed as follows:

By mail:	Assistant Commissioner for Patents Box Patent Extension Washington, D.C. 20231
By FAX:	(703) 308-6916 Attn: Special Program Law Office
By hand:	One Crystal Park, Suite 520 2011 Crystal Drive Arlington, VA

Telephone inquiries related to this notice should be directed to Karin Tyson at (703) 306-3159.

Hiram H. Bernstein
Senior Legal Advisor
Special Program Law Office
Office of the Deputy Assistant Commissioner
for Patent Policy and Projects

cc: Ronald L. Wilson, Director
Health Assessment Policy Staff
Office of Health Affairs (HFY-20)
Food and Drug Administration
5600 Fishers Lane, Room 15-22
Rockville, MD 20857

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Health Assessment Policy Staff
Office of Health Affairs (HFY-20)
Food and Drug Administration
5600 Fishers Lane, Room 15-22
Rockville, MD 20857

RE: rFIX